REMARKS

Reconsideration of the rejections set forth in the Office action mailed July 1, 2004 is respectfully requested. Claims 8-14 were cancelled in the response to restriction requirement filed July 2, 2003, and claim 5 is cancelled with this response. Claims 1-4, 6-7 and 15-16 are currently pending.

I. Amendments

Claim 1 is amended to incorporate the language of previous claim 5.

Claims 1 and 15 are amended to recite that, in the minimally cross-hybridizing set, a duplex consisting of a word of the set and the complement of any other word of the set contains a number of mismatches that is either 1, 2 or 3 less than the length of the word, as recited in the specification at, for example, page 4, lines 32-33.

The recitation in claim 1 that the oligonucleotide tag precursors are of the same length is supported at page 6, line 29 of the specification.

Claim 6 is amended to clarify the meaning of "across said word", in accordance with the specification at page 12, lines 29-30.

No new matter is added by any of the amendments.

II. Incorporation by Reference

At page 4, lines 23-26, applicants' specification incorporates by reference three documents, including a U.S. Patent and an allowed U.S. application (serial no. 08/659,453, which has since issued as U.S. Patent No. 5,846,719. Applicants note that "essential material" can be incorporated by reference in such a manner (MPEP §608.01(p)(I)(A)).

However, the Examiner asserts that the documents "have been improperly incorporated by reference" because the language of the specification fails to "specify what specific information applicant seeks to incorporate by reference" and to "teach with detailed particularity just where that specific information is to be found in each of the cited documents".

The applicants do not agree that their specification "fails to specify what specific

information applicant seeks to incorporate by reference", since it states: "the term 'word' means an oligonucleotide selected from a minimally cross-hybridizing set of oligonucleotides, as disclosed in .... which references are incorporated by reference" (page 4, lines 23-26).

With respect to the alleged requirement that the specification must "teach with detailed particularity just where that specific information is to be found in each of the cited documents", Applicants can find no support for such a standard in the guidelines provided in the MPEP. The MPEP states (§608.01(p)(I)(A)) that "attention *should* be directed to specific portions of the referenced document..." (emphasis added). However, there is no indication that citation of specific portions of a referenced document is required, or that failure to cite specific portions of the document amounts to "improper incorporation by reference", or negates any effect of the incorporated documents, as the Examiner is asserting. The description of "Improper Incorporation" on the same page of the MPEP (8th ed., Rev. 2, page 600-83) refers **only** to "essential material...improperly incorporated by reference to a foreign application or patent or to a publication" (rather than to a US patent).

The Examiner cites language from *Advanced Display Systems Inc. v. Kent State University*, 54 USPQ2d at 1679 (Fed Cir. 2000) in support of his position. However, upon reading this case, the several other cases cited (*In re Severksy, In re Saunders, National Latex Products, and In re Lund*), and additional cases concerned with incorporation by reference, applicants find that none of them support this draconian standard for "proper" incorporation by reference. None of them found incorporation by reference to be "improper" for lack of indication of specific portions of a referenced document. In fact, several cases contradict this assertion.

Applicants also note that, as stated in *Atlantic Thermoplastics v. Faytex Corp.*, 974 F.2d 1279, 1281 (Fed. Cir. 1992); *Newell Cos., Inc. v. Kenney Mfg. Co.*, 864 F.2d 757, 765 (Fed. Cir. 1988); and *Texas Instruments v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1567 (Fed. Cir. 1996), "prior decisions of a panel of the court are binding precedent on subsequent panels unless and until overturned *in banc*."

The primary issue (with respect to incorporation by reference) in *Advanced Display Systems* was whether a jury, rather than a judge, could properly determine what material was incorporated by reference into a reference being cited as anticipating.

The decision in that case includes the statement that one must "...clearly indicate where that material is found in the various documents", followed by citations of several earlier cases, which are also reproduced in the Office Action (page 2). However, none of those cases support such a requirement, as discussed below.

In re Seversky is concerned with the difference between incorporating a parent application by reference and merely stating that an application is a continuation-in-part of the parent application:

> ...the parent application, No. 53,255, **contains no "incorporation-by-reference" language whatsoever**. Its only relation to de Seversky (C) is indicated by the simple statement that it is a "continuation-in-part" thereof. That language is insufficient to incorporate any part of de Seversky (C) into the parent case. All it means is that insofar as the disclosure of the parent finds corresponding disclosure in the grandparent, the parent is entitled to the filing date of the grandparent. 35 U.S.C. §120.
>
> Appellant is confusing two distinctly different things: (1) the right to have benefit of the filing date of an earlier application under §120 for subject matter claimed in a later application because that subject matter is disclosed in an earlier application to which "a specific reference" is made--i.e., a reference to the earlier application per se, and (2) the incorporation by reference in an application of matter elsewhere written down (not necessarily in a patent application), for economy, amplification, or clarity of exposition, by means of an incorporating statement *clearly identifying the subject matter which is incorporated and where it is to be found.* [emphasis added]

It is clear from the context of *In re Seversky* that the statement quoted in *Advanced Display Systems*, italicized above, refers to instructing the reader what documents are to be consulted, but does not require the citation of particular locations within such documents.

In *In re Saunders*, similarly, the reference in question was not "incorporated by reference", but was merely "mentioned" or "referred to":

> ...it was the examiner's position that, "Since the (grand)parent application of Hostettler **specifically mentions** Bailey et al. and because Bailey et al. **specifically mention** Roberts et al., Bailey et al. and Roberts et al. are incorporated into the (grand)parent application of Hostettler....**Treating the three references as one,** the examiner held that "the (grand)parent application of Hostettler **anticipates** (35 U.S.C. 102) the claims..." [emphasis added]

The CCPA found that the §102 rejection, based "treating the three references as one", was unsupported.

In re Lund, similar to *In re Seversky*, above, is concerned with the difference between stating that an application is a "continuation-in-part" of another application and incorporating the other application by reference:

> ...the purpose of "incorporation by reference" is to make one document become a part of another document by referring to the form in the latter in such a manner that it is apparent that the cited document is part of the referencing document as if it were fully set out therein.
> [7] Here, however, **we do not think that the single sentence by which Margerison refers to his earlier application-"The present application is a continuation-in-part application of our application Serial No. 763,806, filed September 29, 1958 (now abandoned)" - is sufficient in and of itself to render Example 2 of the abandoned application part of the patent disclosure...** [emphasis added]

Therefore, in *Saunders* and in this case, as in *Seversky*, the reference to the earlier document(s) does not meet the basic threshold of incorporation by reference. Therefore, the question of "clearly indicating where that material is found in the various documents" never

arises.

In *National Latex Products*, a disclosure was found to be properly incorporated by reference:

> ...**the application expressly refers to the Martin patent,** also involved herein, which provides that the matrices or molds are usually made of metal, preferably copper or steel, copper or bronze plated on the inner surfaces and exteriorly coated with a dark, heat-absorbing coating. **Thus by specific reference the Molitor application supplies the necessary disclosure as to the material to be used in constructing the mold. The disclosure of a patent application may be supplemented by reference to another patent.** ***Application of Heritage, 182 F.2d 639, 643, 86 USPQ 160, 164 (CCPA).*** **The reference to the Martin patent in the Molitor specification constituted such a supplement.** [emphasis added]

The language of the Molitor patent (U.S. Patent No. 2,629,134) which refers to the Martin patent is reproduced below (emphasis added):

> **"A suitable apparatus for continuous internal casting is shown in the application of Henry Martin and Paul Rekettye, Serial No. 179,726, filed August 16, 1950,** but while the process is adaptable for use in the machine shown and described therein, it is by no means confined to that or to any particular type of apparatus."

There is nothing in this language which "clearly indicates where that material is found" in the Martin document. This case therefore contradicts, rather than supports, the contention that such an indication is required for "proper" incorporation by reference.

Finally, the applicants refer to two additional cases, one decided before and the other decided shortly after *Advanced Display Systems*, in which prior patents were found to be

properly incorporated by reference into the patent at issue, via language similar to that employed by the applicants.

In *Nike Incorporated V. Wolverine World Wide, Inc., Brooks Shoe, Inc., and Brooks Sports, Inc.*, 43 F3d 644, 30 Fed.R.Serv.3d 458, 33 USPQ2d 1038 (Fed. Cir. 1994), disclosure of patents incorporated by reference was also used in construction of claims:

> ....as the court recognized, the '304 patent [U.S. Patent No. 4,817,304] states that preferred materials and gases for use in the recited insert are described in U.S. Patents 4,183,156 and 4,219,945 to Rudy, which were incorporated by reference into the '304 patent.
> ...The district court determined that "the claim properly construed requires that the insert be pumped, swollen or distended with a gaseous medium and that 'inflated' would not include air which is merely contained or trapped." Nike, 869 F.Supp. at 812. We agree with the court's analysis, which is supported by the '304 patent specification, **the Rudy patents referenced therein**, and the plain meaning of the term "inflated." [emphasis added]

Language in the '304 patent referencing the "Rudy patents" is as follows:

> ...none of the prior art fluid-filled sole structures met with any commercial success or substantial use until the development of the sole structure as disclosed in U.S. Pat. Nos. 4,183,156 and 4,219,945 of Marion F. Rudy. ...
> The sole structure disclosed in the '156 and '945 Rudy patents overcame the unreliability obstacle through the use of a novel membrane and gas combination. The sole structure in the '156 and '945 patents forms an inflatable insert or insole barrier member of an elastomer material...
> The absence of foam within the gap reduces the weight of the midsole, improves flexibility, and enhances the diffusion pumping process when the membrane/gas combination disclosed in the Rudy patents is used. ...

In a preferred form of the invention, insert 20 is formed of a material as disclosed in the aforementioned Rudy patents and the gas is selected from the group of gases likewise mentioned **in aforementioned Rudy patents, the disclosures of which are hereby incorporated by reference. ...**
As disclosed in the Rudy '945 patent, elastomeric foam materials from which the foam encapsulating member can be made include...

Nowhere does this language "teach with detailed particularity just where that specific information is to be found in each of the cited documents"; yet the Federal Circuit clearly found the Rudy patents to be properly incorporated by reference.

In *Telemac Cellular Corporation v. Topp Telecom, Inc.*, 247 F.3d 1316, 58 USPQ2d 1545 (Fed. Cir. 2001), the disclosure of a patent incorporated by reference was also used in construction of claims:

We note that the informal invention disclosure appears to have yielded yet another Telemac document of record before the district court, U.S. Pat. No. 5,325,418 ("the '418 patent"), owned by Telemac and **incorporated by reference into Telemac's '100 patent. When a document is "incorporated by reference" into a host document, such as a patent, the referenced document becomes effectively part of the host document as if it were explicitly contained therein.** *Advanced Display Sys., Inc., v. Kent State Univ.*, 212 F.3d 1272, 1282, 54 USPQ2d 1673, 1679 (Fed. Cir. 2000); cf. *Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 1381, 53 USPQ2d 1225, 1229 (Fed. Cir. 1999....**In the '418 patent,** as in the informal invention disclosure, the tracking and accounting unit is described....Therefore, **the '418 patent supports the court's conclusion** that a Call Detail Record necessarily includes a listing of charges for calls categorized into the four claimed categories. [emphasis added]

The language used in U.S. Patent No. 5,577,100 ("the '100 patent") with respect to "the '418 patent" is reproduced below (emphasis added):

> The mobile telephone accounting protocol is similar to that described in **U.S. Pat. No. 5,325,418, which is incorporated herein by reference**. In the referenced patent, an accounting system is described which has particular application to a rental phone system or a controlled phone system, such as an intra-corporate system where periodic calculation of phone charges are made prior to receipt of billings from public or switched service providers. ...
> The mobile phone unit of this invention can be used with a mobile phone rental system as described in reference U.S. Pat. No. 5,325,418. ...
> To be functional, the phone unit is programmed and this may be accomplished individually, as described in U.S. Pat. No. 5,325,418 or in batch mode as described in the referenced application. ...

Nowhere does this language "teach with detailed particularity just where that specific information is to be found in each of the cited documents"; yet the Federal Circuit clearly found this patent to be properly incorporated by reference.

To reiterate, the Examiner asserts that documents incorporated by reference in a specification that does not "teach with detailed particularity just where that specific information is to be found in each of the cited documents" are "improperly incorporated". However, the applicants can find no basis for this assertion in the MPEP or in the above-described body of Federal Circuit case law. As shown above, the findings of several Federal Circuit cases contradict this assertion.

II. Rejections under 35 U.S.C. §112, First Paragraph

Claims 1-7 and 15-16 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner states that the "aspect of being able to accurately and reproducibly identify 'minimally cross-hybridizing sets of oligonucleotides' is critical to the claimed method", and repeats the assertion that the documents cited on page 4, lines 24-27 are "improperly incorporated by reference".

The assertion with respect to the incorporated references has been traversed above in Section II.

Even without the disclosure of the incorporated references, the present specification clearly defines a "minimally cross-hybridizing set" (page 4, lines 28-34):

> In such a set, a duplex or triplex consisting of a word of the set and the complement of any other word of the same set contains at least two mismatches. Preferably, a duplex or triplex consisting of a word of the set and the complement of any other word of the same set contains an even larger minimum number of mismatches, e.g. 3, 4, 5, or 6, depending on the length of the words. Still more preferably, the minimum number of mismatches is either 1, 2, or 3 less than the length of the word. Most preferably, the minimum number of mismatches is 1 or 2 less than the length of the word.

"Words", minimally cross-hybridizing sets of words, and tags prepared from such sets are further described in the specification at page 2, lines 17-29 and at page 7, line 21 to page 9, line 2.

The applicants also disclose that preferred sets of tags include those whose perfectly matched duplexes have approximately equal stability, and refer to published sources of methods of determining duplex stability (page 9, second full paragraph). The Examiner contends that these embodiments are not adequately described. However, the MPEP, in its description of determining adequacy of written description, cites case law in stating that "Information which is well known in the art need not be described in detail in the specification" (8th ed., Rev. 2, page 2100-170) and that "What is conventional or well known to one of ordinary skill in the art need

not be disclosed in detail. ... If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met" (8th ed., Rev. 2, page 2100-172). The applicants contend that one of skill in the art at the time of filing the application would have been familiar with the variables involved in duplex stability.

The decision of *University of California v. Eli Lilly and Co.*, cited in the Office Action (page 6), found that the disclosure of an amino acid sequence did not provide adequate written description to support a claim directed to a DNA encoding that sequence. Because the sequence of the claimed DNA was presumably not "conventional or well known to one of ordinary skill in the art" at the time of filing of that application, this case does not appear to be pertinent to the instant application.

With respect to claims 15 and 16, the specification clearly describes the composition of the repertoire of oligonucleotide tags contained within the cloning vectors (e.g. page 7, second full paragraph) and how to prepare such tags (e.g. the methods of Figs. 1 and 2, described on pages 10-14 of the specification), and it further states at page 6, lines 26-28, that the "repertoire of oligonucleotide tags of the desired length contained in the final amplicon may then inserted into a convenient cloning vector". The specification thus establishes that the applicants had possession of the claimed invention. Because cloning vectors per se were conventional to one skilled in the art at the time of filing, there is no need for applicants to provide a detailed description of all possible cloning vectors.

In view of the foregoing, the applicants submit that the pending claims comply with the written description requirements of 35 U.S.C. §112, first paragraph.

III. Further Rejections under 35 U.S.C. §112, First Paragraph

Claims 1-7 and 15-16 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and use the invention without undue experimentation.

The Examiner asserts, firstly, that "Disclosures critical to enabling the claimed method are not properly incorporated by reference". As discussed in detail above, the applicants do not

agree that these references are "not properly incorporated by reference". Moreover, even if these references were not incorporated into the present disclosure, their content was still available to one skilled in the art at the time of filing of the application. The "scope of enablement...is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation" (*National Recovery Technologies, Inc., v. Magnetic Separation Systems, Inc.*, 166 F.3d 1190, 49 USPQ2d 1671, Fed. Cir. 1999). The "purpose of the enablement provision is to assure that the inventor provides sufficient information about the claimed invention to allow a person of skill in the field of the invention to make and use it without undue experimentation, relying on the patent specification and the knowledge in the art" (*Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 1001, 1006, Fed. Cir. 1991).

Regarding the length of the oligonucleotide tags in the repertoire (Item 12 of the Office Action, page 8) being "virtually any length", the independent claim has been amended to specify that the tags have "a predetermined length in the range of from 18 to 60 nucleotides", as recited in original claim 5. Although the specification notes that "reliable synthesis of tag complements that exceed 40-50 nucleotides in length becomes increasingly difficult" (page 8, lines 16-17), it states this in the context of the tradeoff between the size of the tag repertoire and the accuracy of synthesis (page 8, lines 19-20). That is, if a very large repertoire of tags is desired, e.g. for sorting a large number of fragments, a larger number of tag sequence errors would have to be tolerated. However, there is no indication that tags up to 60 nucleotides in length are not useful. Moreover, the methods of the invention are effective to minimize the presence of failure sequences in tags, as described, for example, at page 3, line 25 to page 4, line 5.

With respect to the use of the tag repertoires, the background of the specification notes in general the use of oligonucleotide tags for "tracking, retrieving, and identifying compounds" (page 1, third paragraph), which was known in the art at the time of filing. The advantages of "word"-based tags, whose use was also known in the art, are noted at page 2, lines 16-30. The present invention provides an improvement on the prior art embodiments of "word"-based tags, by providing improved methods of preparing the tags to minimize sequence errors. Because such tag sets had been shown to be useful for sorting and sequencing, even without the improvements first disclosed in the present specification, one skilled in the art would be able to

use the tag repertoires of the invention.

In view of the foregoing, the applicants submit that the pending claims comply with the enablement requirements of 35 U.S.C. §112, first paragraph.

IV. Rejections under 35 U.S.C. §112, Second Paragraph

Claims 1-7 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner's points are addressed as follows.

The phrase "the same minimally cross-hybridizing set" in claim 1 has been amended to "a minimally cross-hybridizing set", thus eliminating the need for antecedent basis.

Claim 7 has been amended to add the term "nucleotides", to clarify the recitations of length.

In view of the foregoing, the applicants submit that amended claims 1 and 7, and their dependent claims, comply with the requirements of 35 U.S.C. §112, second paragraph.

V. Rejections under 35 U.S.C. §102(b)

Claims 15-16 were rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,604,097 (Brenner). This rejection is respectfully traversed for the following reasons.

A. The Invention

The applicants' invention, as embodied in claim 15, provides a repertoire of cloning vectors for attaching oligonucleotide tags to polynucleotides, wherein each of the vectors comprises a double stranded element corresponding to an oligonucleotide tag of the form:

$$w_1(N)_{x1}w_2(N)_{x2} \ldots (N)_{xn-1}w_n$$

wherein

each of w_1 through w_n is a word consisting of an oligonucleotide having a length from three to fourteen nucleotides or basepairs and being selected from a minimally cross hybridizing set, wherein a word of the set and a complement of any other word of the set has a number of mismatches that is either 1, 2 or 3 less than the length of the word;

N is a nucleotide;

each of x_1 through x_{n-1} is an integer selected from the group consisting of 0, 1, and 2,

provided that at least one of x_1 through x_{n-1} is 1 or 2; and

n is an integer in the range of from 4 to 10.

In the oligonucleotide tags shown in the claim, "**at least two words...are separated by one or two nucleotides**" (page 4, lines 6-7).

Such tags can be produced, for example, by the method described on pages 11-12 and illustrated in Fig. 1A, where the length of "(N)k" is "the length of the protruding strand resulting from cleavage with the preferred type of IIs restriction endonucleases" (page 11, lines 21-23).

B. The Prior Art

By citing commercially provided vectors, containing, for example, various polylinkers, promoters, and selection regions, the Examiner appears to suggest that essentially any oligonucleotide would include the recited features of the oligonucleotide tags of the claim. The Examiner asserts that "these limitations" simply "relate to how the repertoire of cloning vectors are to be made". The applicants respond that the limitations are in fact structural limitations which distinguish the tags of the claims from the essentially random collection of oligonucleotides in the cited structures.

One such limitation is that "each of w_1 through w_n is a word consisting of an oligonucleotide having a length from three to fourteen nucleotides or basepairs and being selected from the same minimally cross hybridizing set, wherein a word of the set and a complement of any other word of the set has a number of mismatches that is either 1, 2 or 3 less than the length of the word". This is clearly a structural requirement, and not just a description of how the oligonucleotide tag is made.

In accordance with a further structural feature, at least two such "words" in the oligonucleotide must be "separated by one or two nucleotides" (as described above).

The Examiner counters this argument by asserting that it is not a claimed feature, stating that "the value of x_1 through x_{n-1} can be zero". This does not take into account the further claim language which specifies that "**at least one of x_1 through x_{n-1} is 1 or 2**".

There is no evidence in the cited reference that the oligonucleotides contained in the vectors therein have the claimed structural features. Accordingly, the applicants request that the rejection be withdrawn.

VI. Conclusion

In view of the foregoing, the applicants submit that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

Respectfully submitted,

Date: Nov. 1, 2004

LeeAnn Gorthey
Registration No. 37,337

Correspondence Address:
PAYOR NUMBER 22918
PHONE: (650) 838-4403
FAX: (650) 838-4350